CAP REPORT

NUMBER 11

Drugs and the Third World:

Pizotifen Double Standards in Marketing

CONSUMERS' ASSOCIATION OF PENANG

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Drugs and the Third World:

Pizotifen Double Standards in Marketing

CONSUMERS' ASSOCIATION OF PENANG

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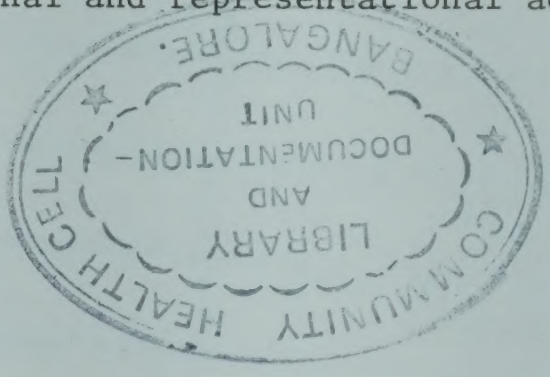

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PREFACE

Pizotifen, an antihistamine drug which is being used for the treatment of migraine in developed countries, is being marketed as an appetite stimulant for children in Malaysia.

It is obvious that drug companies are practising double standards in the promotion and marketing of their products. While pizotifen is promoted as an appetite stimulant for children in developing countries, in developed countries detailed information is provided warning doctors against using the drug in minor ailments or for young children.

The *Drug Index for Malaysia and Singapore* lists two pizotifen preparations. Both are classified as Group C Poisons, meaning that according to the law, they can be sold as dispensed medicines by a pharmacist with entry in the Prescription Book. However, CAP staff have been able to purchase one of them over the counter without even an entry in the Prescription Book.

This report hopes to alert consumers to the dangers of using pizotifen as an appetite stimulant, as well as show them the unethical marketing practices adopted by drug manufacturing companies in developing countries like Malaysia.

The Health Ministry must act immediately to protect the health of all Malaysian consumers. It should remove all pizotifen preparations currently on sale and ban the further use of the drug.

S M Mohd Idris, JP
President
Consumers' Association of Penang
July 1986

Update

This report was presented to the Ministry of Health, Malaysia, in July 1986. On 5 October 1986, the Director of Health, Tan Sri Abdul Khalid, announced that pizotifen, together with six other drugs, has been banned in Malaysia. Manufacturers and distributors would be given three months' grace to withdraw all products containing pizotifen from the market.

CHAPTER 1

INTRODUCTION

Many dangerous and unnecessary pharmaceutical drugs which are banned or severely restricted in developed countries are still being widely marketed and used in developing countries. A study conducted by CAP on the antihistamine drug, pizotifen, has found that this drug is being marketed in Malaysia for children, specifically as an appetite stimulant.

According to the *Drug Index for Malaysia and Singapore (DIMS)* there are two brands of pizotifen on the market. Although both are supposed to be Group C Poisons, CAP staff have been able to purchase one of them, Mosegor, manufactured by Wander, over the counter. Our study shows that there are double standards in the marketing of this drug preparation in Malaysia as compared to the marketing in the UK.

In the UK, the pharmaceutical company, Wander promotes this drug specifically for migraine, unlike in Malaysia where the drug is promoted as an appetite stimulant for children. In the UK and European countries the drug companies provide detailed information, warning doctors

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against prescribing any drug for minor ailments or for use in young children. However, in Malaysia the same companies recommend the drugs in *DIMS* for minor ailments.

Clearly some drug companies are taking advantage of the fact that local monitoring and surveillance of drugs are inadequate and hardly existent. The double standards practised by drug companies in marketing their drugs in Malaysia and other Third World countries can lead to wrong drug prescription and drug use.

Developing countries like Malaysia, which already have limited funds available for the provision of adequate primary health care, should not be spending money on unnecessary drugs.

The Social Audit, a UK public-interest group, produced an anti-advertisement in June 1985 where it argued that the Swiss-based multinational drug company, Sandoz, and the US-based Merck Sharp and Dohme (MS & D), both promote their drugs unethically and operate clear double standards between their First and Third World markets.

In a recent press release by Social Audit (24.6.85) they have called for the withdrawal of two drugs which are heavily being promoted as appetite stimulants in countries where hunger is endemic. According to Social Audit, children in Asia, Latin America and Africa are the principal target for Sandoz's appetite stimulant Mosegor and MS & D's Periactin - the companies' brand names for

pizotifen and cyproheptadine.

In the press release, Sandoz claims that Mosegor is 'highly effective' with 'significant weight gain in 9 patients out of 10' in developing countries. However in Europe - where the company markets pizotifen for migraine treatment under a different brand name (Sanomigran) - their promotional literature claims that weight gain is negligible: 'a slight increase in body weight is observed in some patients'.

According to Charles Medawar, Director of Social Audit and co-author of the anti-advertisement: 'There is absolutely no justification for promoting Pizotifen and Cyproheptadine as appetite stimulants. Hunger is the main health problem in developing countries. With upwards of 800 million malnourished people in the Third World, appetite stimulants are a complete irrelevance. Hungry people need food, not drugs. Medical experts agree that little or nothing is gained by artificially stimulating appetite. Prescribing these tonics for any patient anywhere is rarely if ever justified.'

CAP therefore urges the Ministry of Health to immediately recall all drug preparations containing pizotifen currently on sale, and ban the use of the drug for the safety and health of all Malaysian consumers, especially the children.

CHAPTER 2

PIZOTIFEN: INN (International Nonproprietary Name Selected By WHO)

Pizotifen has antihistamine as well as antiserotinin activity (Bowman, et al, 1980: 12.21-22). Clinical trials suggest that it is an effective prophylactic treatment but is of no value in treating an acute migraine attack (Rogers, et al, 1981: 276). It has sedative and antidepressant actions like those of the tricyclic antidepressants, which it resembles in structure (Bowman, et al, 1980: 12.21-22).

Pizotifen resembles methysergide (a drug used for migraine prophylaxis) and has been used occasionally with some success in the prophylaxis of migraine (Ibid: 16.42). It is given in a dose of 0.5 mg daily, increasing slowly up to 3 mg daily in divided doses (Rogers, et al, 1981: 276).

(1) Adverse Reactions

Pizotifen has similar properties and effects generally associated with the antihistamines. Its most common effect is sedation, varying from slight drowsiness to deep sleep, and includes inability to concentrate,

lassitude, dizziness, hypotension, muscular weakness and incoordination. Other side effects include gastro-intestinal disturbances such as nausea, vomiting, diarrhoea or constipation, and epigastric pain *(Martindale* 28th ed: 1294).

Pizotifen can also produce headache, blurred vision, tinnitus, elation or depression, irritability, night-mares, anorexia, difficulty in micturition, dryness of the mouth, tightness of the chest, and tingling, heaviness, and weakness of the hands. In infants and children, pizo-tifen may act as a cerebral stimulant and symptoms of overdosage may include convulsions and hyperpyrexia. Increased appetite and weight gain may occur (Ibid).

Pizotifen is not listed in the 1979 edition of the *Physicians' Desk Reference*. This means that the drug has been removed from the US market since then.

Of 47 patients with severe migraine given 1 to 2 mg of pizotifen daily, adverse effects were recorded in 22 patients. These reactions included weight increase (15), muscle pain or cramps (3), heavy legs or restless legs (3), fluid retention (3), drowsiness (2), more frequent milder headaches (2), facial flushing (1), reduced libido (1), exacerbation of epilepsy (1), and dreaming (2). Adverse effects necessitating withdrawal from the study occurred in 11 patients (Peet 1977: 192).

(2) *MIMS* Information

In the *Monthly Index of Medical Specialities (MIMS)* Australia (Oct-Nov 1979, Vol 16 No 6: 29) there is one preparation of pizotifen listed:

* Sandomigran (Sandoz)

Indications: Basic and prophylactic treatment of migraine and similar conditions.

Special Precautions: Possible drowsiness; pregnancy; children.

In *MIMS* UK (January 1980, Vol 22 No 1: 73) pizotifen is found as:

* Sanomigran (Wander)

Indications: Prophylaxis of migraine or recurrent vascular headache.

Special Precautions: Drowsiness may occur. Glaucoma urinary retention.

'It is a product which has been recently introduced, and any suspected adverse reactions should be reported to the UK Committee on Safety of Medicines.'

CHAPTER 3

DRUG INFORMATION AND BRANDS SOLD IN MALAYSIA

In Malaysia, doctors obtain information on pizotifen from three major sources. They are:

a) The *Drug Index for Malaysia and Singapore (DIMS)*. *DIMS* is a quarterly publication on ethical medicines available in Malaysia and Singapore. It is prepared by the pharmaceutical companies and distributed free to doctors in both countries.

b) Drug advertisements and brochures which are distributed free to doctors by drug company detailmen.

c) Drug inserts which come together with the drugs when they are purchased. The insert gives information on the use of the drug, the dangers and the precautions to be taken. The instructions and information on the drug insert are provided by the company which markets its particular brand product.

(1) *DIMS* Information

In Malaysia, *DIMS* (Vol 15 No 2 June 1986) lists two

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pizotifen preparations. Both are Group C Poisons which means that they can be sold as dispensed medicines by a pharmacist with entry in the Prescription Book. However, CAP staff were able to purchase one of the drug preparations, Mosegor, over the counter without even an entry in the Prescription Book.

The manufacturers of the pizotifen preparations, together with their contents, are listed in Table I. The manufacturers are both foreign.

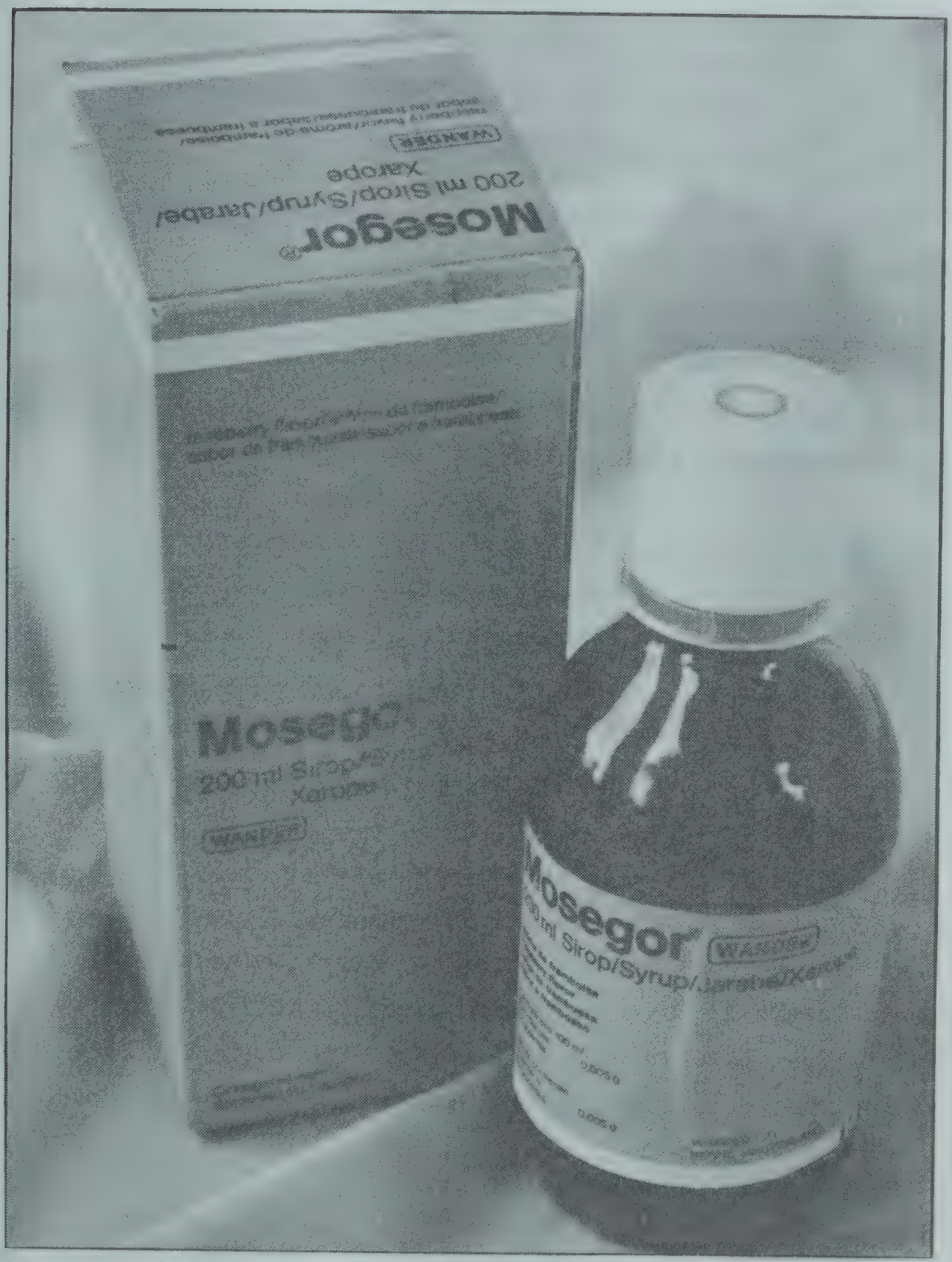
Table I: Pizotifen Preparations Available in Malaysia
Source: *DIMS* June 1986

	Brand Name	Manufacturer	Contents
1.	SANDOMIGRAN	Sandoz	Pizotifen
2.	MOSEGOR	Wander	Pizotifen

(2) Warnings and Contraindications

Under Special Precautions for Sandomigran, information is provided in the following manner:

'Special Precautions: Concurrent administration of



Mosegor raspberry-flavour syrup, containing pizotifen, which was purchased over the counter without an entry in the Prescription Book.

anticholinergic drugs, phenothiazines and butyrophenones. Impaired renal and hepatic function.'

Information on contraindications is provided in the following manner:

'Contra-Indications: Glaucoma and hypertrophy of the prostate.

Under Special Precautions for Mosegor, information is provided in the following manner:

'Special Precautions: Narrow-angle glaucoma, urinary retention. Possible sedative action. CNS-depressive side effects of other drugs and alcohol may be enhanced. Nervousness may occur in children. Pregnant or nursing women.

No contraindications are given.

(3) Indications Given

Besides the lack of information on adverse effects and contraindications, the information given in *DIMS* on drug indications is also very disturbing. The following is information on indications for the brands Sandomigran and Mosegor.

* Sandomigran (Sandoz)

Indications: Basic and prophylactic treatment of migraine equivalents (typical and atypical migraine, vasomotor headache, Horton's syndrome).

Pizotifen also possesses appetite stimulating properties which may lead to an increase in body weight.

* Mosegor (Wander)

Indications: Anorexia in underweight patients; of either organic or psychogenic origins. Mood elevation in the elderly. Also used for the prophylactic treatment of migraine.

(4) Dosages for Children

Of the two brands, only Mosegor indicates dosages for children. Dosages are as follows:

Anorexia: Children - Small initial doses should be gradually increased to an average maintenance dosage of 0.025 mg/kg body weight daily, eg

2-6 years: 5-10 ml syrup or 4-8 drops (0.25-0.5 mg) daily

6-12 years: 10-12 ml syrup or 8-16 drops (0.5-1.0 mg) daily in 2 or 3 divided doses or as directed by the physician.

CHAPTER 4

DRUG INFORMATION INSERT AND BROCHURES

The drug information insert as well as three brochures for the Mosegor brand of pizotifen were examined.

(1) Drug Insert (See Appendix 1)

In the drug insert, Wander recommends Mosegor for 'lack of appetite (anorexia); marked underweight of mental or nervous origin; underweight particularly in convalescence, puberty and in old age and mood disturbances in the elderly'.

However there are no contraindications mentioned.

The precautions to be taken are also not sufficiently stressed. The insert says 'In view of the very slight anticholinergic effect of Pizotifen, caution is required in patients with narrow angle glaucoma (except those successfully treated by surgery) or urinary retention (eg in prostatic enlargement).' Also, 'patients should be warned that, owing to its possible sedative effect, Mosegor may slow their reactions when driving vehicles, operating machinery, etc.' It must be noted that not sufficient emphasis is placed on the dangers of the drug.

In the insert the drug is described as follows: 'Mosegor has an appetite-stimulating action and can thus be used to increase body weight in underweight patients. The compound is well tolerated, permitting safe and specific treatment of anorexia, both in children and adults. In elderly people, Mosegor has been shown to normalise disturbed mood by dejection or oppression, asthenia, anxiety, restlessness, sleep disturbances and impairment of concentration or memory.'

'Owing to its inhibitory effect on biogenicamines, Mosegor may also be used for the prophylactic (interval) treatment of migraine.'

The fact is this drug is an antihistamine and has proved effective only in the prophylactic treatment of migraine. It has no value in the treatment of an acute migraine attack. The drug insert places more stress on its appetite-stimulating action as well as treatment for anorexia. Only secondary importance is placed on its prophylactic treatment of migraine which should not be the case. Medical experts agree that little or nothing is gained by artificially stimulating appetite. Yet this drug is being promoted as an appetite stimulant in developing countries like Malaysia. There is absolutely no justification for promoting pizotifen as an appetite stimulant.

It is clear that multinational drug companies promote their drugs unethically and operate clear double standards

between their First and Third World markets.

Dosage instructions are given as follows:

Children:

'Small initial doses should be gradually increased to an average maintenance dosage of 0.025 mg per kg body weight daily, eg

2-6 years: 5-10 ml syrup (0.25-0.5 mg) daily
6-12 years: 10-12 ml syrup (0.50-1.0 mg) daily in 2 or 3 divided doses, or as directed by the physician.'

Adults:

'Starting with 0.5 mg per day, dosage should be progressively increased up to 0.5 mg three times daily.'

Elderly patients:

'The dosage should be adjusted to individual needs and the severity of the symptoms. A starting dose of 0.5 mg daily is recommended, preferably increasing by 0.5 mg per day. For most patients the daily optimum is 2 to 3 mg in divided doses, but up to 12 mg are well tolerated.

Following improvement, usually within 6 to 8 weeks, gradual reduction or withdrawal of treatment can be attempted.'

There are no known 'Contraindications' for Mosegor.

Under 'Precautions' the following is said:

'In view of the very slight anticholinergic effect of Pizotifen caution is required in patients with narrow angle glaucoma (except those successfully treated by surgery) or urinary retention (eg in prostatic enlargement). However, there have been no reports of untoward reactions in such patients given the recommended dosage, not even in the elderly.

Patients should be warned that, owing to its possible sedative effect, Mosegor may slow their reactions when driving vehicles, operating machinery, etc.

No adverse effects of the compound during pregnancy have been reported. Nevertheless, Mosegor, like other drugs, should only be administered in pregnancy in compelling circumstances. Mosegor should be kept out of reach of children.'

Under 'Interactions' is listed 'Central effects of sedatives, hypnotics, antihistamines, including certain common cold preparations, and alcohol may be enhanced.'

Under 'Side-effects', Wander states that 'Sedation may be experienced at the beginning of treatment, and in some patients this may well be desirable. Otherwise it can usually be avoided by increasing the dosage gradually or reversed by a progressive reduction in dosage. In

high doses Mosegor may cause dryness of the mouth.'

(2) Drug Brochures

CAP staff were able to obtain three different brochures on Mosegor.

* In the first one, it says that 'Anorexia affects growth and health' and one can 'break this vicious circle ... with Mosegor the new and triple active appetite inducer'.

  'Mosegor is a specific appetite stimulant for the treatment of:

  - anorexia
  - lack of desire to eat
  - emaciation
  - underweight

  Mosegor stimulates the appetite in children, adolescents, elderly patients.'

  No 'Side Effects', or 'Precautions' are listed. Instead under 'Tolerance' Wander says 'The tolerance is generally good. Rarely in the beginning of treatment there may be slight sedation. Caution is required in cases of glaucoma and prostatic hypertrophy'. Wander is obviously playing down whatever 'side effects' the drug has.

It also states that Mosegor syrup is available in raspberry and mandarine flavours (See Appendix 2). Clearly Mosegor is being recommended for children.

* In the second brochure (See Appendix 3) Wander says that 'Mosegor gives you the appetite of a lion'. There is a bright coloured picture of a lion licking its mouth at a plate of food in front of it.

On the reverse side is written:

'Pizotifen, substantially different and superior to Cyproheptadine'. Below this is a chart comparing studies of Mosegor and Cyproheptadine on children and adults. There is also an illustration showing body weight increase in children, based on studies carried out in 180 children.

No 'Precautions' or 'Side Effects' are mentioned. Neither is there any information under 'Tolerance' as is listed in the first brochure.

* The third brochure (the most recent distributed to the medical profession) is a four-leaf pamphlet. On the cover are four doll-like figures of increasing sizes. At the top of the cover is stated: 'Lack of appetite ... Mosegor the better solution'.

Inside the pamphlet is written: 'Mosegor the specific appetite stimulating agent

- Stimulates the appetite rapidly

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- Demonstrates statistically significant weight gains
- Shows mood stabilizing effect
- Possesses an excellent tolerability.'

It also quotes results from a study conducted by 'more than 100 established pediatricians' on children and adolescents given Mosegor.

On the back page the 'Side Effects' and 'Precautions' listed are as minimal as the one found in the drug insert.

The brochure also lists syrup and sugar-coated tablets (See Appendix 4).

Undoubtedly Wander, the company which manufactures Mosegor, is deliberately promoting its drug to children in Malaysia, unlike in the UK where it promotes its brand of pizotifen specifically for migraine. The double standards practised in the promotion of this drug in a developing country like Malaysia as compared to a developed country are unwarranted and most undesirable.

CHAPTER 5

CASE REPORT

Although there has been no reported case of pizotifen abuse in Malaysia, the following is a case of cholestatic jaundice, in which the causative agent was pizotyline (pizotifen), a phenothiazine-related drug. The case report was published in an article in the *Archives of Internal Medicine* (Vol 144 April 1984).

The patient's symptoms were compatible with either hepatitis or biliary obstruction. Diagnostic laboratory studies were performed to exclude both of these entities. The history of drug ingestion plus the clinical and histologic features established pizotyline as the causative agent. Pizotyline is indicated in the prophylactic treatment of migraine, headaches and also has appetite-stimulant properties.

The 68-year-old man had been hospitalised in the Philippines for left-sided weakness due to thrombo-ischemic infarct in the right middle cerebral artery. On 20 August 1982 he was transferred to the emergency room of the Long Beach (California) Veterans Administration Medical Center for further medical examination. Jaundice

developed the day before the transfer, and after that the patient also suffered increasing weakness and nausea of two weeks' duration.

The patient had had a history of alcohol abuse. He had lived in the Philippines for the last two years, and he had smoked three packs of cigarettes per day for 30 years. His medical history included a cerebral vascular accident (one month before this admission), hypertension (without medication) and angina of three years' duration (which was relieved by nitroglycerin therapy). The patient and his family denied having had fever, night sweats, abdominal pain, diarrhoea, hematemesis, melena, or contact with a patient with hepatitis. He also denied receiving any blood transfusions in the past. He noted a pruritic rash for the past week. Medication regimen at the time of admission was as follows: ergoloid mesylates, 1 mg three times a day; cyclandelate, 100 mg three times a day; pizotyline (an appetite stimulant similar to cyproheptadine hydrochloride), 25 mg three times a day and dipyridamole, 50 mg twice a day. He had no known drug allergies.

A review of the literature disclosed no reports of cholestatic hepatotoxicity associated with the medication regimen the patient was prescribed during his three-week hospitalization at Long Beach. Before that hospitalization, he had taken only occasional acetaminophen for headache. The patient had no known drug sensitivities or history of alcohol or street drug abuse. Twelve days before the onset of his nausea and jaundice symptoms, pizotyline was

added to the patient's drug regimen as an appetite stimulant. Pizotyline is a tricyclic (benzocycloheptathiophene) compound that possesses structural similarities to the tricyclic antidepressants and phenothiazines. Pizotyline is also chemically and pharmacologically similar to cyproheptadine hydrochloride, sharing both its antihistamine and antiserotonin properties.

In this case, the patient exhibited the clinical features of a phenothiazine-type cholestatic jaundice that include jaundice, fever, nausea, weakness, and a pruritic maculopapular rash with slow resolution of these symptoms. The biochemical abnormalities the patient manifested that were consistent with a phenothiazine-induced cholestasis included increased levels of alkaline phosphatase, serum transaminases, and cholesterol, hyperbilirubinemia and eosinophilia. These biochemical changes resolved gradually during the course of several months. The liver biopsy showed a cholestatic pattern suggestive of a drug-induced toxic reaction. The negative test for hepatitis-associated antigen ruled out viral hepatitis B as a causative factor.

Therefore, it is believed that pizotyline was the causative agent in the development of this patient's cholestatic jaundice. Pizotyline possesses significant structural similarities to the phenothiazines, a group of drugs well-known to cause intrahepatic cholestasis. Usually, discontinuation of the causative agent is the only

treatment required, though some patients may have persistent biochemical abnormalities and jaundice for months to years afterward (Coodley, et al, 1984: 815-817).

CHAPTER 6

CONCLUSION

This report has attempted to make a case for the need to remove all pizotifen preparations from the market.

There is no doubt that pharmaceutical companies are practising double standards by promoting pizotifen as an appetite stimulant for children in Malaysia, whereas in the UK the drug is promoted specifically for migraine.

Wander not only claims that its drug is superior as an appetite stimulant, it is deliberately aiming its product at children. This can be seen from the fact that various paediatric preparations are available, and the studies made were largely conducted on children. The double standards in the promotion of the same drug in a developed country and in a Third World country like Malaysia is most unethical and irresponsible. The Ministry of Health should take immediate action to withold the sale and marketing of the drug in Malaysia and protect the health of our children. Doctors and parents must be warned of the dangers of prescribing this drug to children.

CAP strongly urges the Ministry of Health to immediately

recall the drug from the market, for the safety and health of Malaysian consumers.

CAP would like to repeat its call for the setting up of an independent unit within the Ministry of Health to control and evaluate imported as well as locally manufactured drugs during all stages of manufacture, packing, storage, advertising and distribution of medicines. This body should comprise medical doctors, pharmacists and pharmacologists to look into all the aspects mentioned and to advise legislation along the lines of the Food and Drug Administration (USA), the Committee on Safety of Medicines (UK) and the Expert Committee, Ministry of Health in Bangladesh. It is evident that multinational drug companies adopt lax double standards in their marketing precisely because there are no mandatory requirements for them not to do so. A 'watchdog' committee is urgently required to increase awareness and ensure corporate responsibility.

REFERENCES

1. Bowman, W C and Rand, M J, *Textbook of Pharmacology* 2nd ed 1980, Blackwell Scientific Publications.

2. Coodley, E L, Muro, J and Sato, R I, 'Pizotyline-Induced Cholestatic Jaundice', *Archives of Internal Medicine* Vol 144 April 1984.

3. *Drug Index for Malaysia and Singapore* Vol 15 No 2 June 1986.

4. *Martindale: The Extra Pharmacopoeia,* Twenty-eighth ed 1982.

5. *Monthly Index of Medical Specialities,* Australia October-November 1979 Vol 16 No 6: 29.

6. *Monthly Index of Medical Specialities,* UK January 1980 Vol 22 No 1: 73.

7. Peet, K M S, *Current Medical Research and Opinion* 1977, Vol 5: 192, cf *Martindale: The Extra Pharmacopoeia* 28th ed (1982): 1317.

8. Rogers, H J, Spector R G and Trounce, J R, *A Textbook of Clinical Pharmacology,* 1981 Hoddler and Stroughton.

APPENDIX 1

DRUG INSERT FOR MOSEGOR

Mosegor® WANDER

Composition
Pizotifen (INN rec.) (as the hydrogen malate)

Sugar-coated tablets 0.5 mg
Syrup 0.5 mg / 10 ml

Properties
Mosegor has an appetite-stimulating action and can thus be used to increase body weight in underweight patients. The compound is well tolerated, permitting safe and specific treatment of anorexia, both in children and adults.
In elderly people Mosegor has been shown to normalize disturbed mood by alleviating symptoms such as hopelessness, feelings of dejection or oppression, asthenia, anxiety, restlessness, sleep disturbances, and impairment of concentration or memory.

Owing to its inhibitory effect on biogenic amines, Mosegor may also be used for the prophylactic (interval) treatment of migraine.

Indications
- Lack of appetite (anorexia)
- Marked underweight of mental or nervous origin; underweight particularly in convalescence, puberty and in old age
- Mood disturbances in the elderly

Dosage

Children:
Small initial doses should be gradually increased to an average maintenance dosage of 0.025 mg per kg body weight daily, e.g.:
2– 6 years: 5–10 ml syrup (0.25–0.5 mg) daily
6–12 years: 10–20 ml syrup (0.50–1.0 mg) daily
in 2 or 3 divided doses, or as directed by the physician.

Adults:
Starting with 0.5 mg per day, dosage should be progressively increased up to 0.5 mg three times daily.

Elderly patients:
The dosage should be adjusted to individual needs and the severity of the symptoms. A starting dose of 0.5 mg daily is recommended, preferably increasing by 0.5 mg per day. For most patients the daily optimum is 2 to 3 mg in divided doses, but up to 12 mg are well tolerated.
Following improvement, usually within 6 to 8 weeks, gradual reduction or withdrawal of treatment can be attempted.

Contraindications
There are no known contraindications.

Precautions
In view of the very slight anticholinergic effect of pizotifen caution is required in patients with narrow angle glaucoma (except those successfully treated by surgery) or urinary retention (e.g. in prostatic enlargement). However, there have been no reports of untoward reactions in such patients given the recommended dosage, not even in the elderly.
Patients should be warned that, owing to its possible sedative effect, Mosegor may slow their reactions when driving vehicles, operating machinery etc.
No adverse effects of the compound during pregnancy have been reported. Nevertheless Mosegor, like other drugs, should only be administered in pregnancy in compelling circumstances.
Mosegor should be kept out of the reach of children.

Interactions
Central effects of sedatives, hypnotics, antihistamines, including certain common cold preparations, and alcohol may be enhanced.

Side effects
Sedation may be experienced at the beginning of treatment, and in some patients this may well be desirable. Otherwise it can usually be avoided by increasing the dosage gradually or reversed by a progressive reduction in dosage.
In high doses Mosegor may cause dryness of the mouth.

Instructions for opening
(syrup): The guarantee closure can be removed as shown in the diagram on the box:
1. Remove plastic measuring beaker
2. Tear off perforated strip
3. Remove cap
4. To reclose, replace cap and press on firmly.

® Trade Mark

WANDER LTD BERNE SWITZERLAND

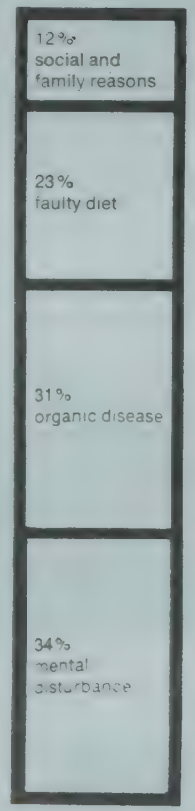
3 815 115.02 DFES
(DR/SI)

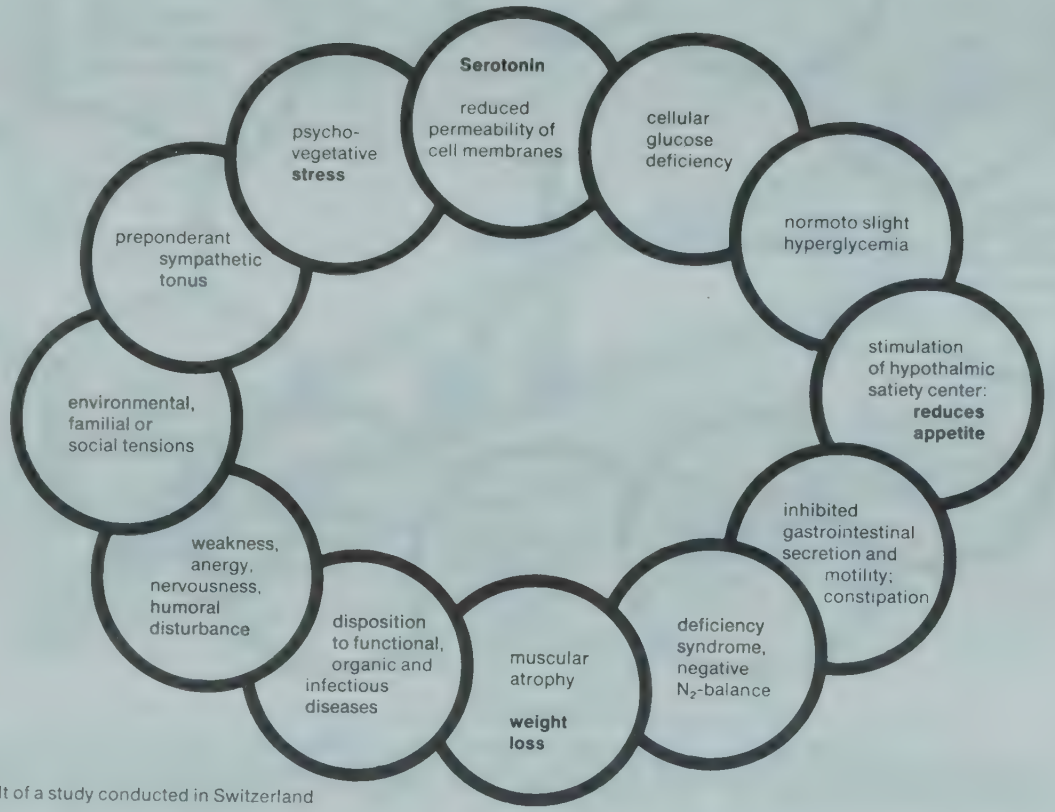
APPENDIX 2

DRUG BROCHURE ON MOSEGOR (I)

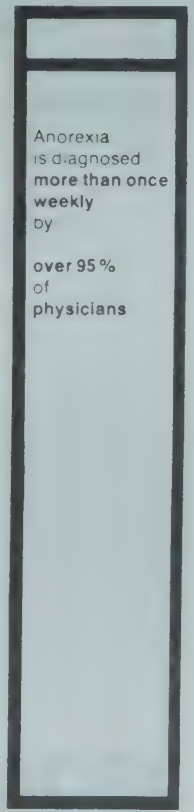
Anorexia affects growth and health

Main causes of anorexia*





Frequency of diagnosis*



*Result of a study conducted in Switzerland

How to break this vicious circle?...

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Logic
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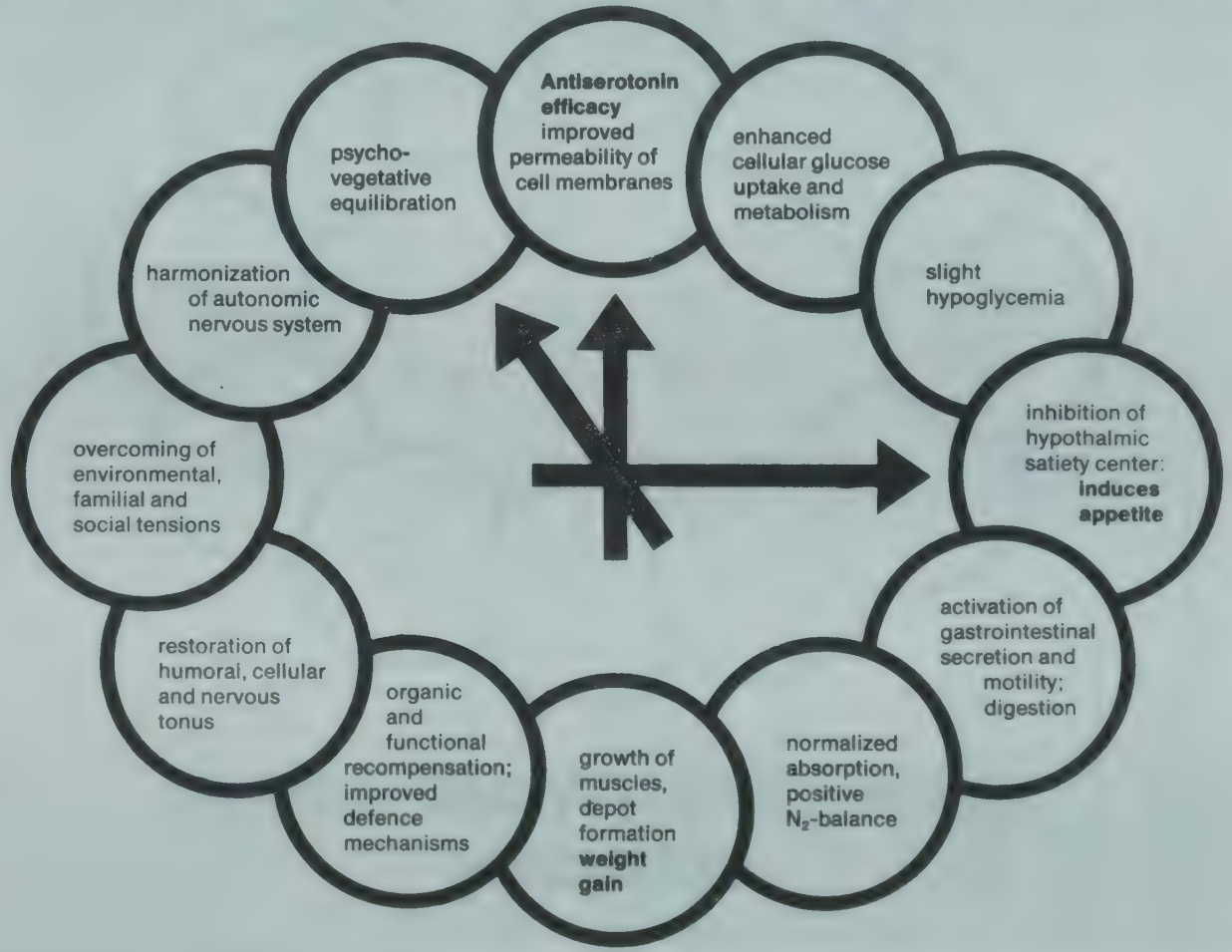
...with Mosegor
the new and triple active appetite inducer



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Mosegor® the specific orexigenic agent from WANDER

Emaciated or underweight patients do not only need a well balanced, complete and acceptable diet.

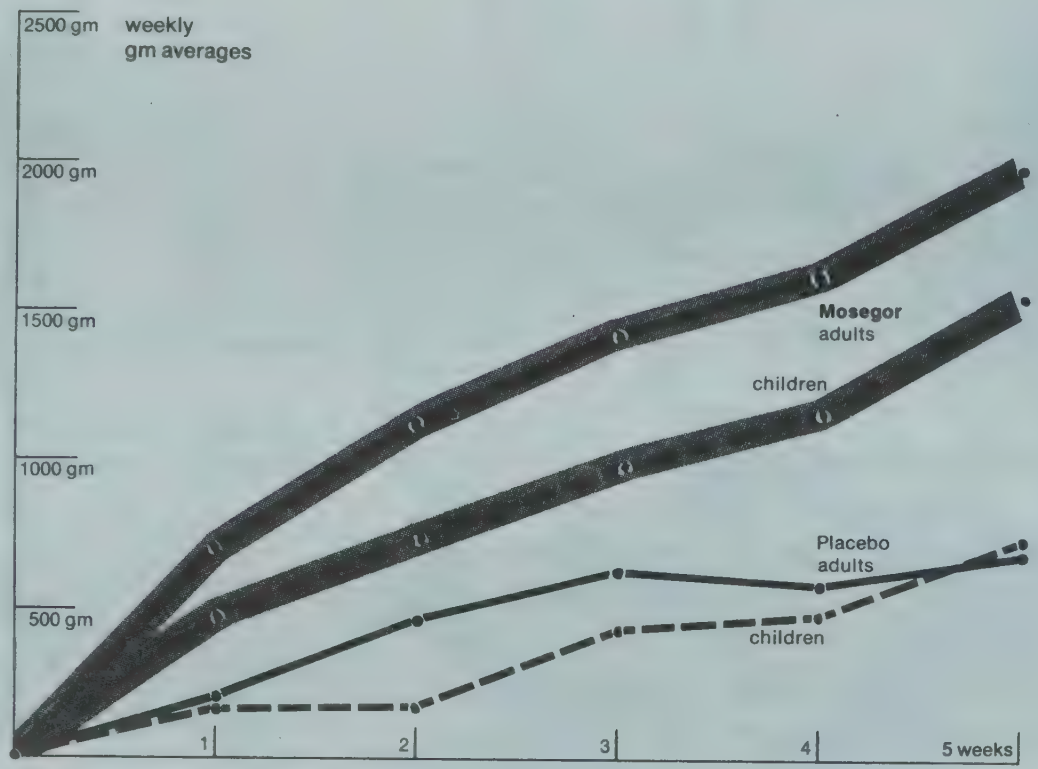
They should also have the necessary appetite.

Mosegor is a specific appetite stimulant

This feature has been demonstrated convincingly and with high statistical significance in 894 patients.

The appetite stimulating action can be best measured by the weekly weight gain.

Results of clinical trial (894 patients)



Double blind trials with placebo and comparable drugs have shown the specific appetite stimulating property of Mosegor in a statistically significant manner. The results are convincing and are valid for children as well as adults.

For the treatment of

- anorexia
- lack of desire to eat
- emaciation
- underweight

continued next page

Mosegor®

WANDER

stimulates the appetite in children, adolescents, elderly patients

Produces regular weight gain in
inappetence
emaciation
underweight

Tolerance
The tolerance is generally good. Rarely in the beginning of treatment there may be slight sedation.
Caution is required in cases of glaucoma and prostatic hypertrophy

Dosage
Children:
0.025 mg/kg body weight

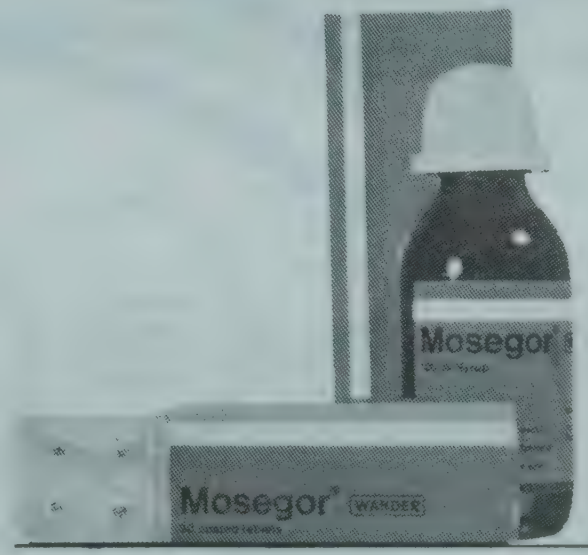
Syrup of 0.25 mg/5 ml
2– 6 years 5–10 ml daily
6–12 years 10–20 ml daily

divided each into 2 to 3 single doses taken before meals

Adults and elderly patients:
1 tablet of 0.5 mg t.i.d.

Composition
Each sugar-coated tablet contains 0.5 mg. pizotifen
Each 10 ml. syrup contains 0.5 mg. pizotifen

Availability
Coated tablets: 30's, 100's and 500's
Syrup: 100 ml. and 200 ml.
(raspberry and mandarin flavours)



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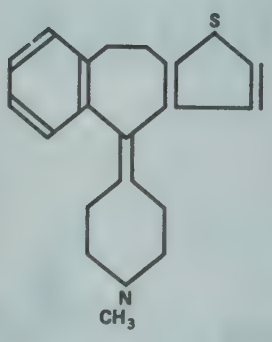
APPENDIX 3

DRUG BROCHURE ON MOSEGOR (II)

DEVELOPED BY
WANDER TO
RESOLVE THE
FREQUENT PROBLEM
OF
LOSS OF APPETITE



Mosegor®

GIVES YOU THE APPETITE OF A LION

WANDER

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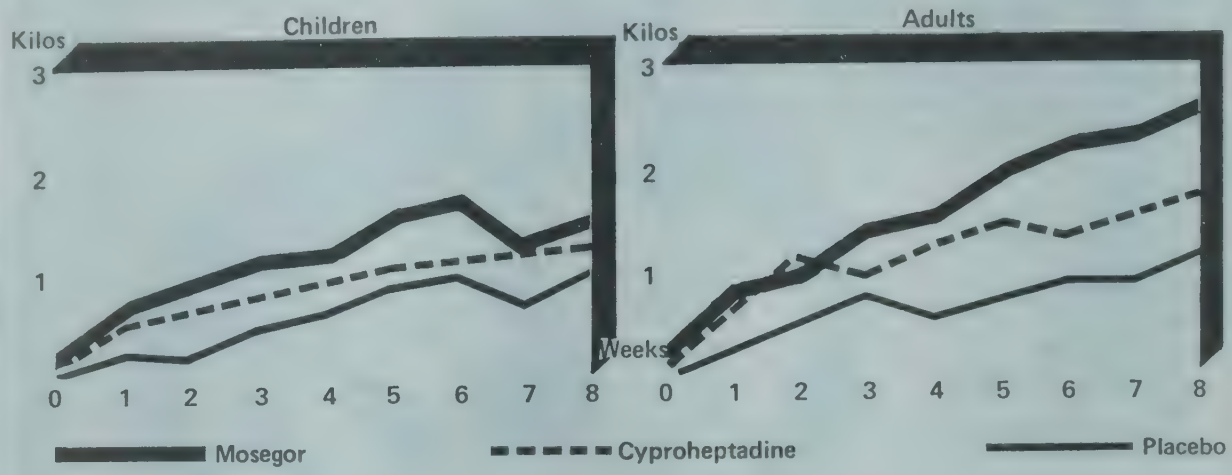
Mosegor®

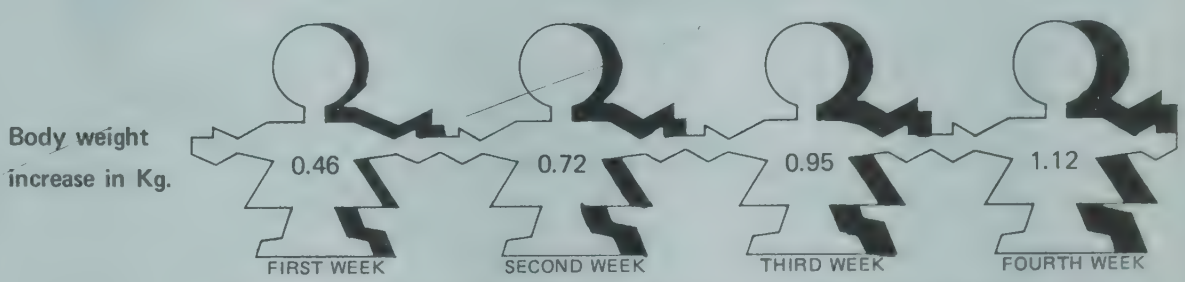
WANDER

Pizotifen, substantially different & superior to Cyproheptadine



Comparative Studies with Mosegor, Cyproheptadine & placebo in 383 patients by various authors*

Rapid onset of action



Results of studies in 180 children according to experiences of several investigators.*

Composition: Pizotifen: 1 coated tablet = 0.5 mg
10 ml syrup = 0.5 mg

Properties : MOSEGOR produces rapid weight gain through increased appetite.

Indications : Anorexia, loss of appetite from any cause.

Dosage : **Adults:** 1 coated tablet 3 times daily.

Children: 2- 6 years 1-2 teaspoons per day
6-12 years 2-4 teaspoons per day
12-16 years 4-6 teaspoons per day
(divided into 2 or 3 single doses)

Presentation : Syrup — 100 ml.
Coated tablets — 30, 100, 500

*BIBLIOGRAPHY REFERENCES
Ch. Blanc, N.B. Blancheti, B. Finelli, D. Jakasa, Th. Kolster, A. Maddedu, J. Rosemberg, Ch. Santana Maia, A. Tsougranis, F. Cardoso Filho, J. De Franco, Martin Du Pan, A. Pardo Gilbert, Es. Sanchez Villares, Ch. Vonda Tsigou.

SANDOZ LTD.
DIVISION)

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APPENDIX 4

DRUG BROCHURE ON MOSEGOR (III)

Lack of appetite

often a problem in the family in children as well as in adults

Mosegor®

the better solution

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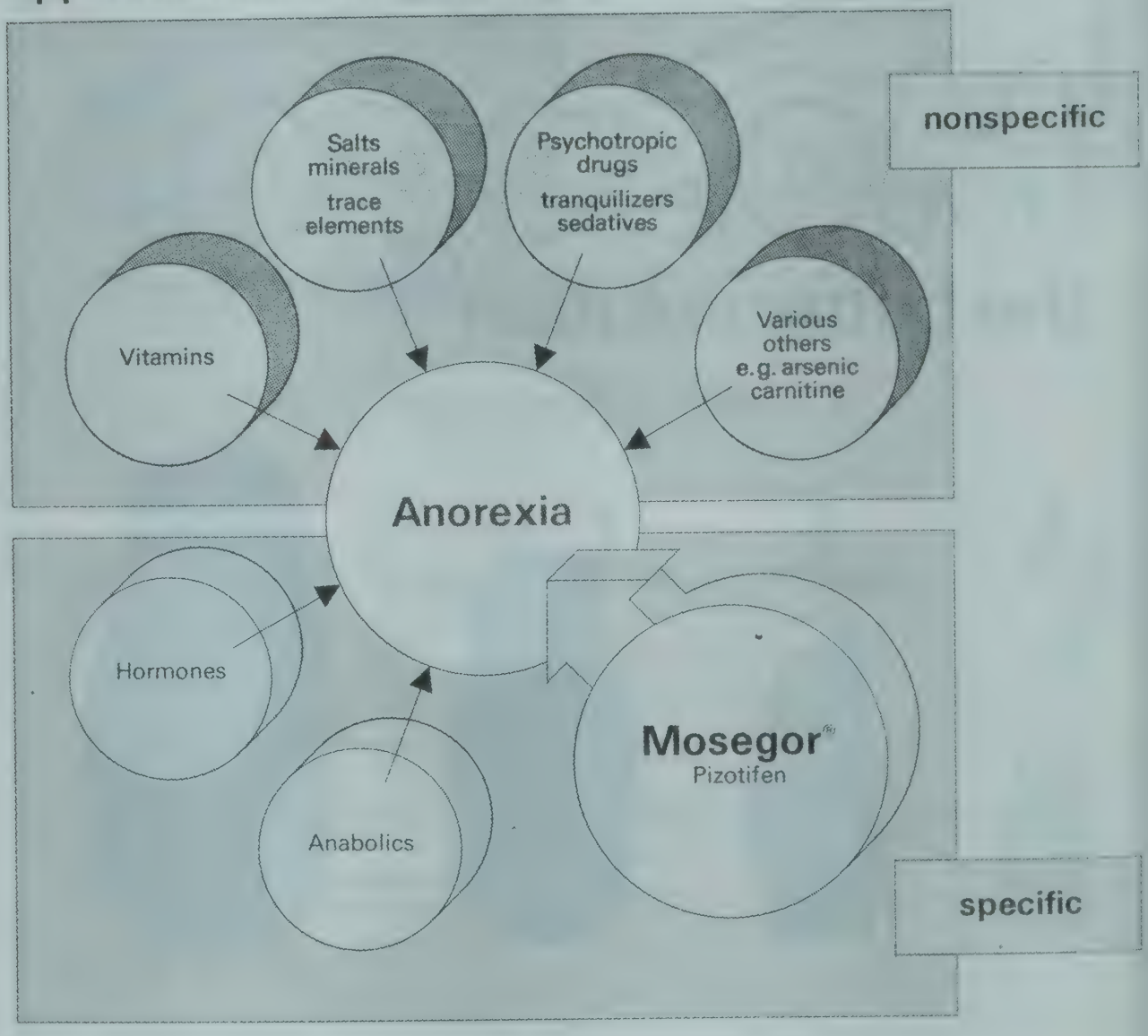
Anorexia represents a frequent therapeutic problem due to

- Disturbances of growth and puberty
- Convalescence
- Familial and social tensions
- Stress situations and nervousness

Appetite stimulating agents



Mosegor allows specific treatment without hormones or anabolics.

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Mosegor® the specific appetite stimulating agent

Stimulates the appetite rapidly

The rapid onset of action has been proven in clinical tests.
The increase of appetite in adults and children appears in the first week of treatment.

Demonstrates statistically significant weight gains

The weight gain during medication, a consequence of improved appetite, is not due to water retention in the tissues, but is the result of a positive nitrogen balance, as shown by Albanese et al.[15].

Shows mood stabilizing effect

Fluctuations of mood, which frequently occur in anorectic patients, are improved or eliminated

Possesses an excellent tolerability

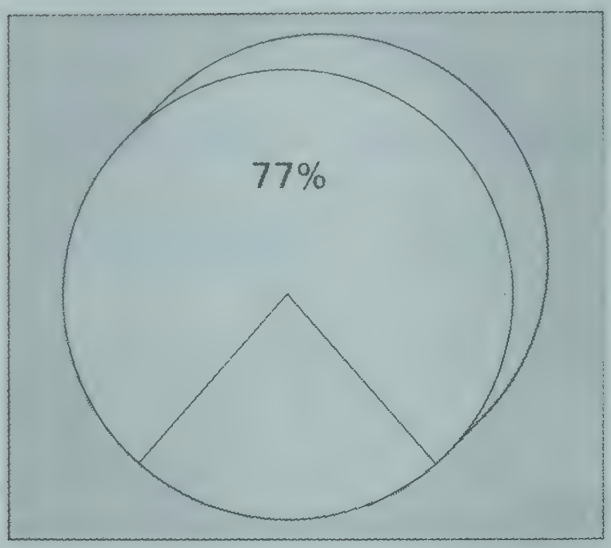
Especially suited for long-term treatment in children and in adults.

continued next page

Clinical evaluation of the action of Mosegor in children and adolescents

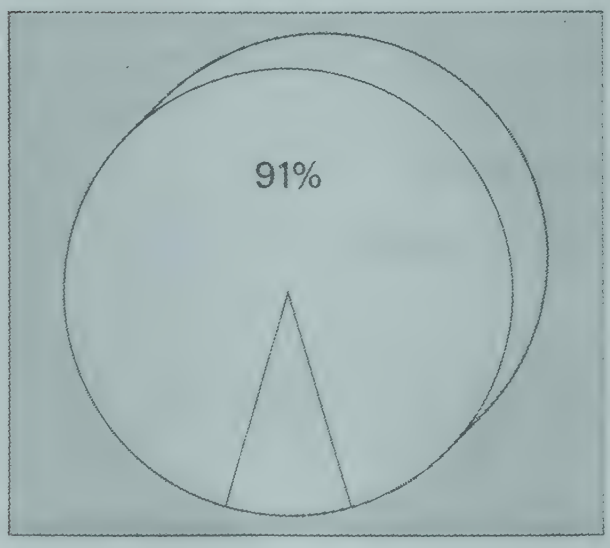
This study[1] with Mosegor was conducted by more than 100 established pediatricians

Number of patients:
906 had 3–4 weeks' treatment,
277 of them continued to
6–8 weeks' treatment



● Stimulation of appetite

In 77% of all cases, the appetite was reported to be very good or good.



● Significant weight gains

In 91% of the treated children a weight gain was observed.

Mean weight gain	
after 3–4 weeks	0.86 kg
after 6–8 weeks	1.09 kg

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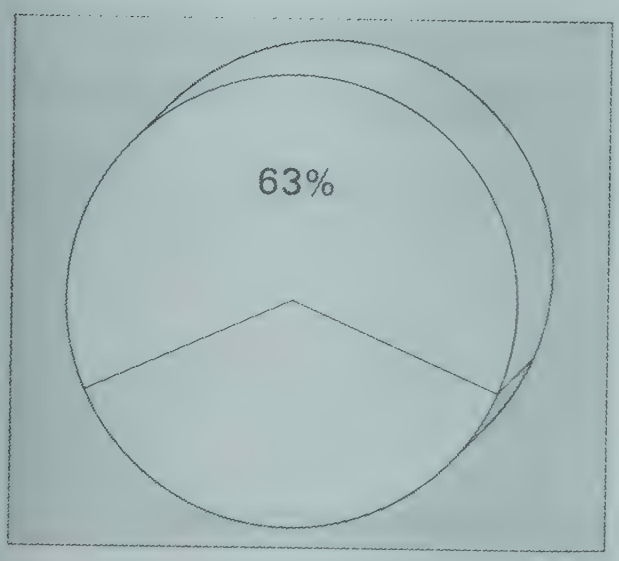
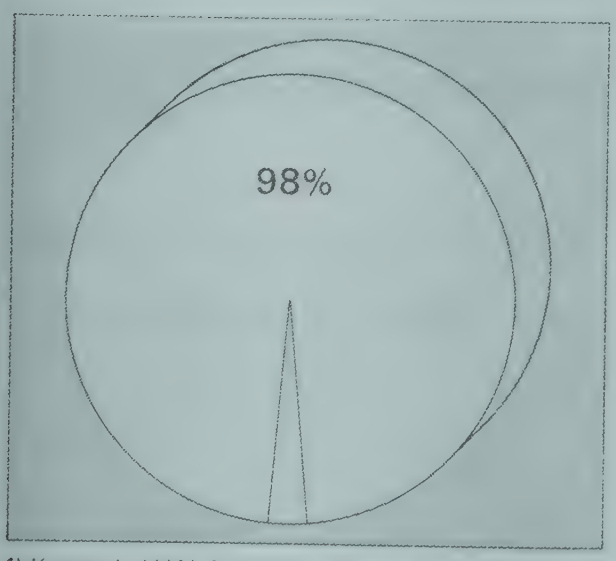
Age of patients:
from 2 to 16 years.
428 of the children were male and
478 female.



Mood stabilizing effect

Mosegor has a favourable effect on mood, which is often disturbed in association with anorexia.
In 63% of the cases with such disturbances, mood was improved or normalized.



1) Krainick, H.W. Aerztliche Praxis 29 (1977)

Excellent tolerability

In 98% of the treated children the tolerability during the treatment was very good or good.
Drowsiness and diarrhea were mostly mild and transient.

Acceptance of the syrups
In 88% of the treated children the acceptance was very good or good.

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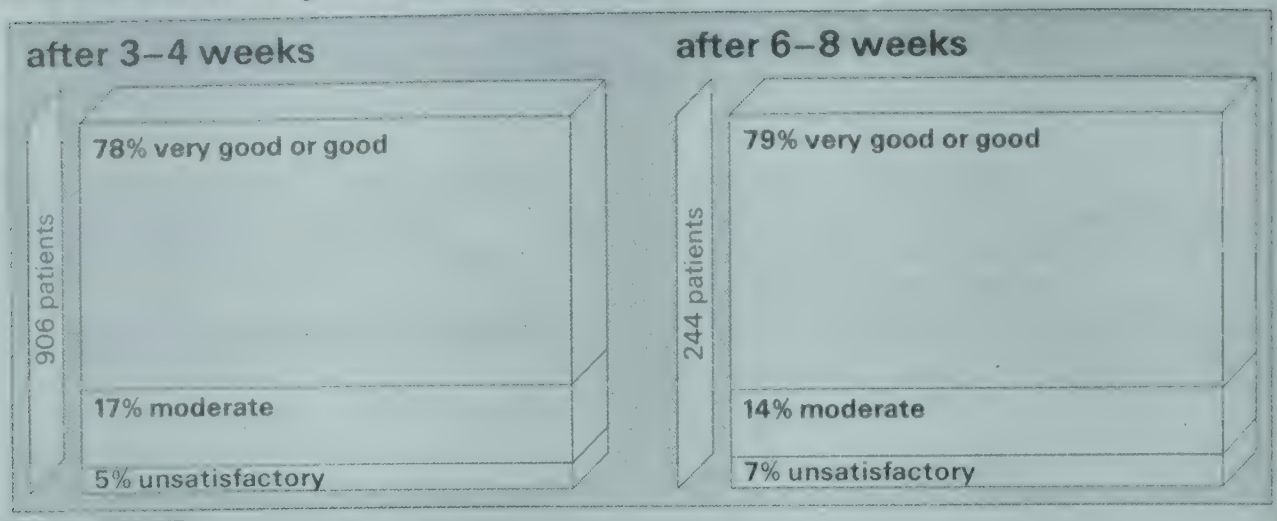
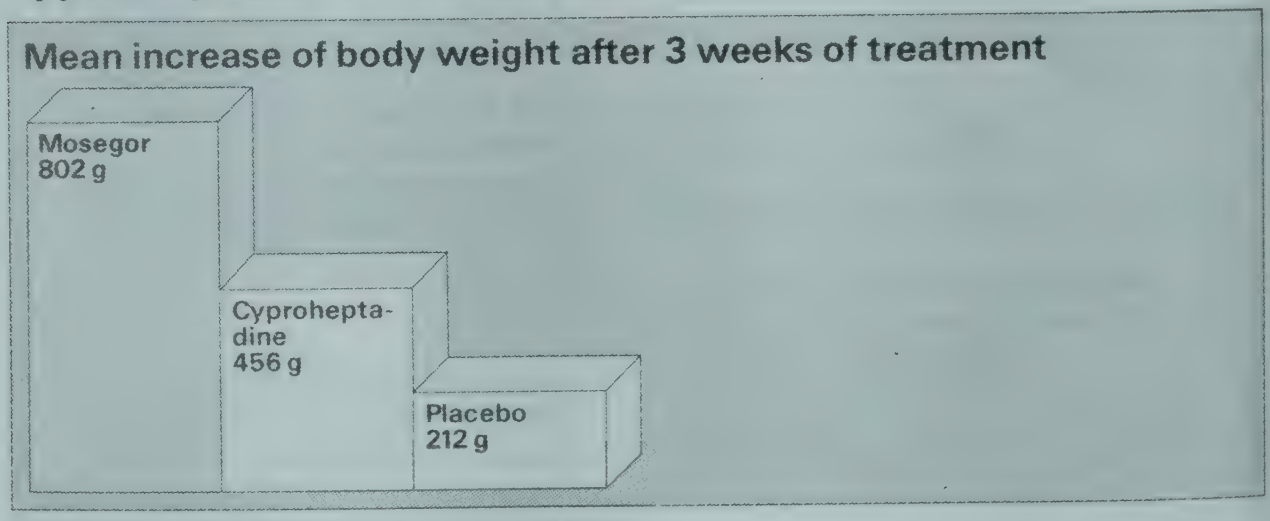
Overall therapeutic evaluation of the study[1)]



1) Krainick, H.W. Aerztliche Praxis 29 (1977)

From a study[2)] concerning a double-blind trial with 45 children suffering from anorexia and underweight:

Increase in body weight with Mosegor compared with cyproheptadine and placebo[2)]



2) Cioffi, E. Acta Pediatrica Latina, 27, 103–118 (1977)

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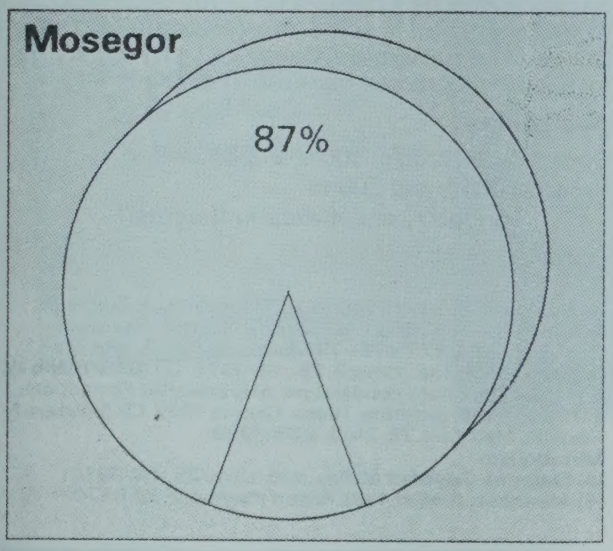
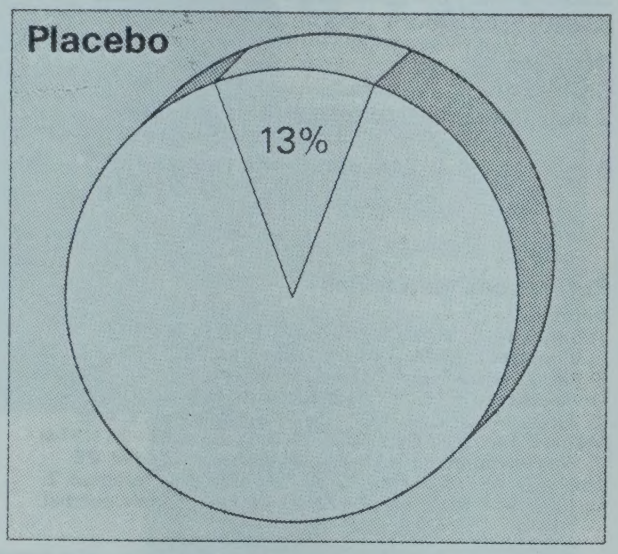
Clinical evaluation of the action of Mosegor in adults

This study[3] concerns a single-blind trial with 31 patients suffering from anorexia and underweight.

Stimulation of appetite (after 3 weeks of treatment)

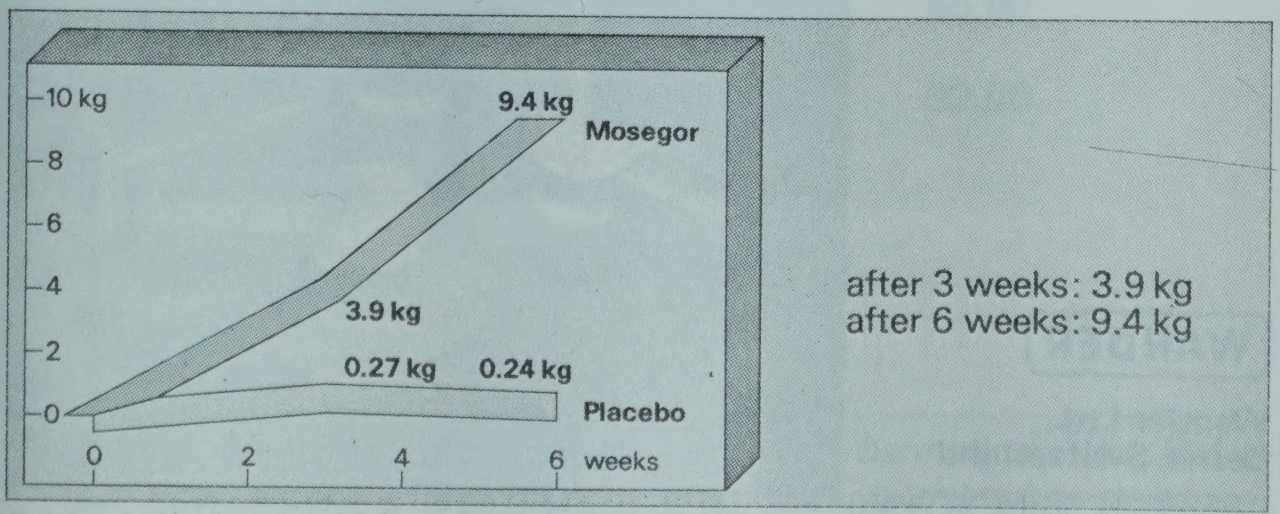


In 87% of the treated patients the appetite was reported to be very good or good.



In only 13% of the patients was the appetite reported to be good.

Average weight increase



3) Sabin, J. et al. Med. Welt (Stuttg.) 29, 445–447 (1978)

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Mosegor® syrup sugar-coated tablets

Composition
Pizotifen:
1 sugar-coated tablet = 0.5 mg
10 ml Syrup = 0.5 mg

Indications
Lack of appetite
Marked underweight of mental or nervous aetiology
Underweight particularly in convalescence, puberty and elderly people.

Dosage
Children:
2 to 6 years: ½–1 teaspoonful twice daily (5–10 ml)
6 to 12 years: 1–2 teaspoonfuls twice daily (10–20 ml)

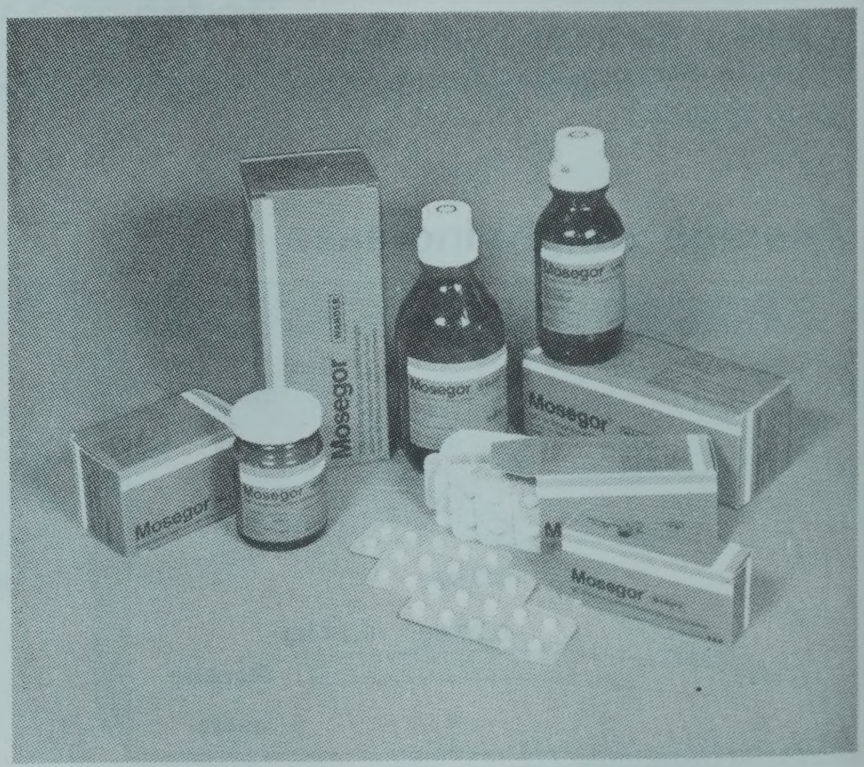
Adults:
2 teaspoonfuls three times daily (30 ml) or
1 tablet three times daily.

Precautions
Caution is required in patients with narrow angle glaucoma or with urinary retention (e.g. prostatic enlargement)

Side Effects
Sedation may be experienced at the beginning of treatment and in some anorectic patients this may well be desirable. Otherwise it can usually be avoided by a gradual increase in dosage.

Availability
Coated tablets: 30's, 100's, and 500's
Syrup: 100ml. and 200ml.
(raspberry and mandarin flavours)

References (additional)
Anorexia
1) **Senesael, L.M.** Ars Med. (Brux.) **7,** 257–261 (1978) 2) **Villanueva, M.M.** Sem. méd. (B. Aires) **148,** 205–211 (1976) 3) **Pieragostini P. and Patane, E.** Acta paediat. lat. (Reggio Emilia) **28,** No. 6 (1975) 4) **Blanchetti, N.B.** Sem. méd. (B. Aires) **145,** 2056–2062 (1974) 5) **Chiorboli, E. and Mega, L.** Rev. bras. Clin. Terapeut. **3,** Suppl. 6, 19–28 (1974) 6) **Westermann, P. and Rossi, M.V.** Minerva pediat. **26,** 486–492 (1974) 7) **Baruffi, W.** Rev. bras. Clin. Terapeut. **2,** No. 6, 275–280 (1973) 8) **Martin du Pan, R.** Helv. paediat. Acta **Suppl. 30,** 28–29 (1973) 9) **Tsougranis, A.** Curr. ther. Res. **14,** 372–375 (1972) 10) **Cardoso Filho, F.** Rev. bras. Clin. Terapeut. **1,** 87 (1972) 11) **Martin du Pan, R. and Ackermann W.** Ther. Umsch. **28,** 415 (1971) 12) **Ackermann W.** Traitement du retard pondéral par anorexie chez l'enfant par un orexigène de synthèse. Thesis, Geneva 1969 13) **Sicuteri, F.** Gazz. int. Med. Chir. **74,** 2103–2116 (1969)
Metabolism
14) **Fraipont-Guyot et al.** Rev. méd. Liège **25,** 414 (1970) 15) **Albanese, A. et al.** Nutr. Report internat. **2,** 29 (1970)



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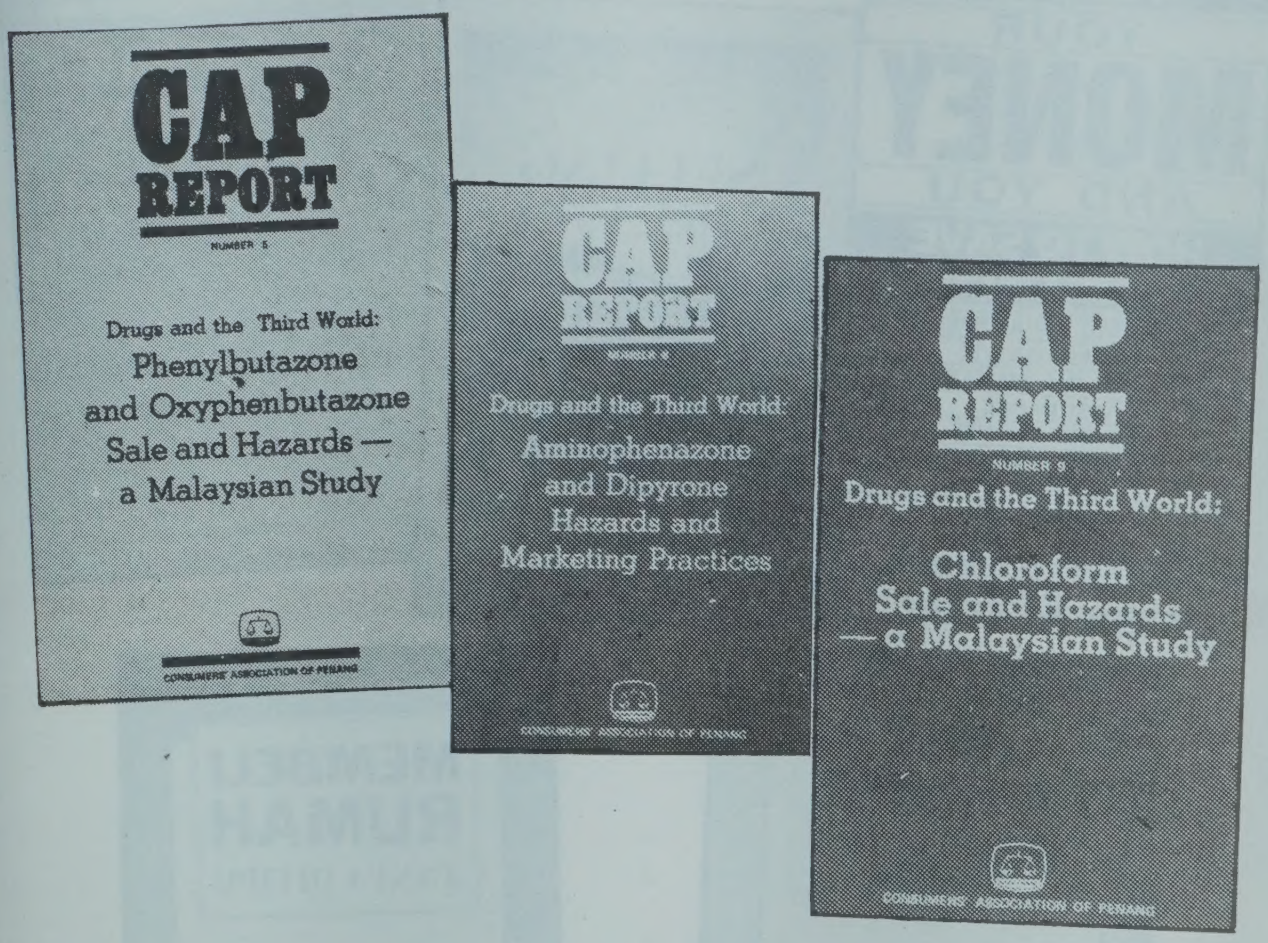

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6)	* Stanozolol	

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* *Besides pizotifen, these drugs were also banned by the Malaysian government a few months after the reports were presented to the Ministry of Health.*

Drugs and the Third World:

Pizotifen Double Standards in Marketing

Pizotifen is an antihistamine drug which is being marketed in Malaysia as an appetite stimulant for children. In the UK, pizotifen is promoted specifically for migraine and is not indicated for the treatment of minor ailments or for use in young children.

This report reveals the unethical marketing strategies employed by drug companies in promoting pizotifen in developing countries. It also urges the Ministry of Health to remove all preparations containing this drug that are on the Malaysian market.

In October 1986, a few months after CAP sent this report to the Malaysian Ministry of Health, the government banned the sale of pizotifen in Malaysia.

The Consumers' Association of Penang (CAP) is a non-profit making organisation which fights for the rights and interests of Malaysian consumers through research, educational and representational activities.

The issues it takes up include the fulfilment of basic needs (food, nutrition, health, housing, transport, etc.), food and product safety, environmental pollution and problems, the rational use of resources, specific problems of women, and business malpractices.

This is part of a series of CAP Reports aimed at providing the public with the results of some of the important areas of CAP's activities. It is hoped that this series will generate public interest and awareness, and help to contribute towards a better life for Malaysians.

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